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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,072	04/03/2007	Siegfried Ansorge	PMP-0003	6887

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EXAMINER	
SIMMONS, CHRIS E	
ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,072	ANSORGE ET AL.	
	Examiner	Art Unit	
	Chris E. Simmons	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/22/2006 09/28/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims: It is acknowledged that claims 2-11 have been amended and claim 12 is newly added by Applicant in the preliminary amendment filed on 8/10/2007.

Information Disclosure Statement

The information disclosure statements filed 06/22/2006 and 09/28/2006 fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

The disclosure is objected to because of the following informalities:

- the term "characterised" is misspelled on page 2 line 20. The correct spelling is "characterized"
- the term "utilisation" is misspelled on page 4 line 10. The correct spelling is "utilization"
- the term "normalisation" is misspelled on page 4 line 22. The correct spelling is "normalization"
- the term "stabilising" is misspelled on page 4 line 24. The correct spelling is "stabilizing"

- the term "sufactant" is misspelled on page 6 line 2. The correct spelling is "surfactant"
- the term "stabilisers" is misspelled on page 2 line 20. The correct spelling is "stabilizers".

The specification contains multiple misspellings. Applicant must analyze the specification and make corrections accordingly.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

The claim recites a method for the treatment of COPD with silibinin, its salts and/or its pro-drugs, and alpha-lipoic acid. There is insufficient written basis for prodrugs of cisplatin in the specification.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert.*

denied, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.I "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5,2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure ..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties of prodrugs of silibinin, aside from a broad recitation that such are contemplated for use in the invention. As such, it is not apparent that Applicant was actually in possession of, and intended to be used within the context of the present invention, any specific prodrugs of silibinin at the time the present invention was made.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 provide for the use of silibinin with lipoic acid, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In this case, the limitation, "...silibinin, it salts and/or its pro-drugs with alpha-lipoic acid" as recited is indefinite. One could reasonably interpret this to mean that the pro-drug is some conjugate of silibinin and alpha-lipoic acid (i.e., silibinin and its pro-drug with alpha-lipoic acid; or a) a pro-drug of silibinin and b) alpha-lipoic acid.

Claim Rejections - 35 USC § 101

Claims 1-11 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by 6,262,019 ('019).

The instant claim reads on a method for the simultaneous, separate or timed cytoprotective treatment of chronically obstructive lung diseases comprising administering silibinin, its salts and/or its pro-drugs with alpha-lipoic acid.

'019 teaches in claims 1, 3, 21, and 24 a composition comprising sylmarin (i.e., silibinin) and lipoic acid used for treating emphysema, a COPD disease. It further teaches in col. 2, lines 25-31, pulmonary diseases are among the disease associated with reduced glutathione levels; and in claim 23 it teaches the systemic administration to

treat various pulmonary diseases. The comprising language of the instant claims allows for the presence of other essential ingredients in the '019 patent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 12 is rejected under 35 USC 103(a) as being unpatentable over Engelen et al. ("Altered Glutamate Metabolism Is Associated with Reduced Muscle Glutathione Levels in Patients with Emphysema"; Am J Respir Crit Care Med. 2000 Jan;161(1):98-103.) in view of US Patent 6,262,019 ('019).

Determination of the scope and content of the prior art (MPEP 2141.01)

Engelen et al. discloses that emphysema, a COPD, is associated with depleted glutathione (GSH) values (page 100, 1st sentence under *DISCUSSION*).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Engelen et al. does not expressly disclose the treatment of COPD using a combination of alpha-lipoic acid and silibinin.

Finding of prima facie obviousness

'019 discloses in claims 1, 3, 21, and 24 a composition comprising sylmarin (i.e., silibinin) and lipoic acid used for treating emphysema, a COPD disease. It further discloses in col. 2, lines 25-31, pulmonary diseases are among the disease associated with reduced glutathione levels; and in claim 23 it discloses the systemic administration to treat various low glutathione-related diseases, including pulmonary diseases, such as the COPD, emphysema.

The comprising language of the instant claims allows for the presence of other essential ingredients in the '019 patent.

At the time of the invention it would have been obvious to a person of ordinary skill in the art to treat COPD with a combination therapy using alpha-lipoic acid and silibinin.

Rational and Motivation (MPEP 2142-2143)

The suggestion/motivation for doing so would have been to increase the amount of glutathione in those suffering from disease associated with depleted glutathione levels using a known combination therapy for increasing glutathione..

Therefore, it would have been obvious to combine the teachings in each reference to obtain the invention as specified in claim(s).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim 12 is rejected under 35 USC 103(a) as being unpatentable over US Patent 6,495,170 ('170) in view of US Patent 6,262,019 ('019).

Determination of the scope and content of the prior art (MPEP 2141.01)

'170 discloses that silymarin (i.e., silibinin) is an enhancer of glutathione regeneration (col. 6, lines 64-66).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

'170 does not expressly disclose the treatment of COPD using a combination of alpha-lipoic acid and silibinin.

Finding of prima facie obviousness

'019 discloses in claims 1, 3, 21, and 24 a composition comprising sylmarin (i.e., silibinin) and lipoic acid used for treating emphysema, a COPD disease. It further discloses in col. 2, lines 25-31, pulmonary diseases are among the disease associated with reduced glutathione levels; and in claim 23 it discloses the systemic administration to treat various low glutathione-related diseases, including pulmonary diseases, such as the COPD, emphysema.

The comprising language of the instant claims allows for the presence of other essential ingredients in the '019 patent.

At the time of the invention it would have been obvious to a person of ordinary skill in the art to treat COPD with a combination therapy using alpha-lipoic acid and silibinin.

Rational and Motivation (MPEP 2142-2143)

The suggestion/motivation for doing so would have been to increase the amount of glutathione in those suffering from disease associated with depleted glutathione levels using a known combination therapy for increasing glutathione..

Therefore, it would have been obvious to combine the teachings in each reference to obtain the invention as specified in claim(s).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re*

Opprecht 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim 12 is rejected under 35 USC 103(a) as being unpatentable over Valenzuela et al., ("Selectivity of Silymarin on the Increase of the Glutathione Content in Different Tissues of the Rat"; Planta Med 1989; 55: 420-422) in view of US Patent 6,262,019.

Determination of the scope and content of the prior art (MPEP 2141.01)

Valenzuela et al. discloses that silibinin increases total glutathione content in various organ systems (abstract).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Valenzuela et al. does not expressly disclose the treatment of COPD using a combination of alpha-lipoic acid and silibinin.

Finding of prima facie obviousness

'019 discloses in claims 1, 3, 21, and 24 a composition comprising sylmarin (i.e., silibinin) and lipoic acid used for treating emphysema, a COPD disease. It further discloses in col. 2, lines 25-31, pulmonary diseases are among the disease associated

with reduced glutathione levels; and in claim 23 it discloses the systemic administration to treat various pulmonary diseases. The comprising language of the instant claims allows for the presence of other essential ingredients in the '019 patent.

At the time of the invention it would have been obvious to a person of ordinary skill in the art to treat COPD with a combination therapy using alpha-lipoic acid and silibinin.

Rational and Motivation (MPEP 2142-2143)

The suggestion/motivation for doing so would have been increase the level of glutathione in the body of a subject suffering from depleted glutathione levels.

Therefore, it would have been obvious to combine the teachings in each reference to obtain the invention as specified in claim(s).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chris E. Simmons whose telephone number is (571) 272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chris Simmons
Patent Examiner

AU 1614

September 20, 2007

Ardin H. Marschel 9/29/07
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SUPERVISORY PATENT EXAMINER

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